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10/532,067	12/28/2005	Gerd Sutter	GRUE-004	6100

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EXAMINER	
HURT, SHARON L	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
10/27/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,067	SUTTER ET AL.	
	Examiner	Art Unit	
	SHARON HURT	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 6-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2 and 6-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendments to the claims filed June 27, 2008 have been acknowledged and entered. Claims 20-21 are newly added.

Status of the Claims

Claims 1-2, 6-19 and new claims 20-21 are pending. Claims 3-5 have been cancelled. Claims 1-2 and 6-21 are under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1-2 and 6-19 under 35 U.S.C. 103(a) as being unpatentable over Yang et al. (Vaccine, 1997, Vol. 15, No. 12/13, pages 1303-1313) in view of Kumar et al. (Immunology Letters, April 2002, Vol. 81, pages 13-24) and Bujard et al. (WO 98/14583, 1998) **is maintained for claims 1-2, 6-21.**

The claimed invention is drawn to a recombinant Modified Vaccinia Vaccine Ankara (MVA) virus comprising at least one nucleic acid coding for a *Plasmodium falciparum* merozoite surface protein-1 (MSP-1) protein or fragment or mutein, wherein the fragment is p83, p30, p38, p33, p19 or p42, wherein the mutein is differentiated from the MSP-1 sequence by addition, deletion, insertion, inversion and/or substitution of one or more amino acids, wherein

the MSP-1 protein is of the isolate 3D7 or the FCB1 strain, wherein the MSP-1 is reduced in its adenine thymine (AT) content. The claimed invention also is drawn to a method of production of the recombinant MVA virus comprising the steps: (a) transfecting a eukaryotic host cell with a transfer vector, wherein the transfer vector comprises a nucleic acid encoding a *Plasmodium falciparum* merozoite surface protein-1 (MSP-1) protein or a fragment or a mutein, wherein the mutein differs by the addition, deletion, insertion, inversion and/or substitution of one or more amino acids from the MSP-1 sequence, wherein the nucleic acid is flanked by MVA sequences 5' and/or 3', wherein the sequences are suitable for the homologous recombination in the host cell; (b) infection with a virus based on MVA, preferably MVA; (c) cultivation of the host cell under conditions suitable for homologous recombination; and (d) isolation of the recombinant virus based on MVA, wherein the virus is isolated from the culture supernatant or from the cultivated host cells.

The claimed invention is also drawn to a vaccine comprising the recombinant MVA virus and a pharmacologically compatible carrier, wherein the vaccine further comprises a MSP-1 fragment or a mutein and/or a nucleic acid coding for MSP-1, or a fragment or mutein, wherein the constituents can be administered simultaneously, sequentially or separate, wherein the vaccine does not comprise and adjuvant, wherein the vaccine further comprises a recombinant MSP-1 protein. The claimed invention is also drawn to a method for the prophylaxis and/or therapy of malaria comprising administering the recombinant virus, MSP-1, a fragment or a mutein and/or a nucleic acid coding for MSP-1, or a fragment or mutein, wherein the transfer vector comprises a selection marker.

Yang et al. teaches a recombinant vaccinia virus encoding a *Plasmodium falciparum* merozoite surface antigen (MSA1) (p. 1303, Abstract). A highly attenuated strain of vaccinia virus, Modified Vaccinia Ankara (MVA) was developed as an expression vector and shown to be equivalent to replication competent vaccinia virus in several vaccine models (p. 1311, last paragraph). The merozoite surface complex is processed into fragments, 30, 38 and 42 k Da (p. 1304, top of left column). Each gene was inserted into the thymidine kinase region of the vaccinia virus, under the control of the synthetic strong early/late promoter (p. 1303, Abstract). The effect of signal and anchor sequence on the biochemical processing and antibody response to the C-terminus region of the MSA1 is expressed by recombinant vaccinia virus (p. 1304, left column). BSC-1 cells, a eukaryotic host cell was transfected with a transfer vector, a recombinant vaccinia virus which encodes a *Plasmodium falciparum* MSA1 (p. 1305, left column). Insertion of the sequence, under transcriptional control of the promoter, provides a visual marker for identification (p. 1304, last paragraph). The MSA1 fragments contain the 108 bp region directly downstream from the signal sequence and an additional 2 bp on the 5' end of the C-terminal to preserve the reading frame (p. 1305, Table 1). The vaccinia virus thymidine kinase sequences flanking the vaccinia genome (p. 1304, last paragraph). The virus containing the MSA1 was determined by SDS gel electrophoresis from the cell pellets and 50X concentrated supernatants (p. 1308, left column). Yang teaches a vaccine composition complete with Freund's adjuvant administered to monkeys, mice and rabbits in one vaccine or in two parts (p. 1304, 1st paragraph). Yang also teaches a vaccine composition that does not comprise adjuvant (p. 1307, 3rd paragraph). The vaccines were administered to mice for the prophylaxis of malaria with the recombinant vaccinia virus vaccine (p. 1308, right column).

Yang does not teach the recombinant vaccinia virus MSP-1 protein is from the 3D7 or FCB1 strain of *P. falciparum* or a MSP-1 with reduced AT content.

Kumar et al. (hereinafter Kumar) teaches about a DNA plasmid vaccine encoding the merozoite surface protein 1 (MSP-1) from the 3D7 strain of *Plasmodium falciparum* (Pf3D7) (Abstract). Kumar also teaches about the construction of a vaccinia recombinant expressing MSP-1 (page 15, Section 2.2).

Bujard et al. (hereinafter Bujard) teaches a Malaria, *Plasmodium* species, which is stabilized by a process characterized by a reduction of the AT content (page 6, 3rd full paragraph). Bujard teaches vaccine carriers, viral carriers including vaccinia (page 13, 2nd full paragraph). Bujard also teaches processing fragments p83, p31, p36, p30 and p19 (page 15, last paragraph).

The combination of references suggests the claimed invention.

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use the 3D7 strain of Kumar. The person of ordinary skill in the art would have been motivated use the 3D7 strain because a plasmid constructed with the human strain 3D7 would be a good vaccine candidate, and reasonably would have expected success because of the results of Kumar and the teachings of Yang.

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use a reduced AT content. The person of ordinary skill in the art would have been motivated to make that (those) modification(s) because Bujard teaches it stabilizes the vaccine, and reasonably would have expected success because of the teaching of Yang and Bujard.

Response to Arguments

Applicant's arguments filed June 27, 2008 have been fully considered but they are not persuasive. Applicants argue "Yang merely mentions MVA in the context of concerns regarding the safety of live virus as a vaccine vector." Applicants also argue "Yang merely states that a "highly attenuated strain of vaccinia virus, Ankara (MVA), has been developed as an expression vector and shown to be equivalent to replication competent vaccinia virus in several vaccine models"." It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use a MVA vector. The person of ordinary skill in the art would have been motivated to use a MVA vector because Yang teaches it is highly attenuated and has been successful in vaccine models.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON HURT whose telephone number is 571-272-3334. The examiner can normally be reached on M-F 8:00 - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Hurt

October 15, 2008

/Bruce Campell/

Supervisory Patent Examiner, Art Unit 1648